

From: [James Swenberg](#)
To: [Ravi Subramaniam/DC/USEPA/US@EPA](#)
Subject: Re: half-life question
Date: 05/03/2012 03:35 PM
Attachments: [Half-life slide.pptx](#)

No, half of the adducts were lost in the first 6 hours. This was not repair, it was cell death. The initial calculation of the remaining loss gave a half-life of 94 hours. This came down to 63 hours when all samples were evaluated. I am attaching a slide of the data.

Jim

On 5/3/2012 3:26 PM, Ravi Subramaniam wrote:

Thanks. Just to make sure I am interpreting correctly. The 63 hour half life (with n=5) was for the first part of the elimination? But with n=3 that half-life was 6 hours?

Ravi.

Ravi Subramaniam
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From: James Swenberg <jswenber@email.unc.edu>
To: Ravi Subramaniam/DC/USEPA/US@EPA
Date: 05/03/2012 03:08 PM
Subject: Re: half-life question

Our 10 ppm study showed that half of the adducts were lost in the first 6 hours after a single 6 hr exposure, based on an n=3. We completed the analysis with n=5 and found that the half live was 63 hours. This (10 ppm) is a toxic exposure, so we have now completed the exposures in a 28-day rat study with sacrifices at 1, 2, 3 and 4 weeks of exposure to 2 ppm, 7 days/week, but have not gotten to the DNA adduct analyses,. This study also has a half-life study with -6 and -24 hours, 3 days and 7 days post exposure. It should provide definitive information on the adduct half-life under non-cytotoxic conditions. I have a new postdoc starting in mid August, who will work on this study. I forwarded your earlier questions to Tom Starr, so that I also get his input. He only used the 94 hour data in the Tox Sci paper. I hope this helps clarify things.

Jim

On 5/3/2012 2:04 PM, Ravi Subramaniam wrote:

Hi Jim:

Sorry to have these questions trickling in. . .

Lu (unpublished) indicated a biphasic decay curve for the adduct--a rapid loss followed by a slow process corresponding to a half-life of 94 hours. (Swenberg et al. 2011, pg S134).

However in calculating steady state concentrations, only the slow process appears to be included (pg S135, second column).

Ravi.

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